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Atty. Docket No. HESP0010U-US
Serial No: 09/575,377Amendments to the Claims

51. (Previously amended) A method for identifying one or more ion channels of a cell that may be affected by a test substance by deconvoluting a change in cell membrane potential, comprising:

exposing a test substance to a system,

in which said system comprises:

(a) a solid state microelectrode array;

(b) a serum-free cell culture comprising one or more electrically active cells having a cell membrane including one or more ion channels, which cells are capable of providing a measurable action potential that exhibits changes in one more perceptable characteristics selected from after potential, time to cessation of activity, frequency, amplitude, shape, spike rate, or time constant in response to a test substance;

(c) an intervening layer that is acting as a high impedance seal and which is positioned between said microelectrode and said one or more cells of said cell culture,

(d) accompanying deconvolution software with instructions that can be implemented by a computer to deconvolute changes in the action potential of the cells upon exposure to the test substance, wherein the deconvolution analysis does not include a spectral analysis that makes use of a Fourier transformation, and performing a deconvolution analysis to identify an ion channel affected by said test substance.

52. (Previously Amended) The method of claim 51, wherein the one or more

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characteristics exhibited by said action potential is manifested in its waveform or a derivative thereof.

53. (Previously Amended) The method of claim 52, in which the one or more characteristics include at least one of time to cessation of activity, frequency, amplitude, or shape.

54. (Previously Added) The method of claim 51, in which the instructions comprise data processing instructions capable of receiving input data comprising data on ion flux through ion channels selected from the group consisting of sodium channels, potassium channels, calcium channels, and combinations thereof.

55. (Previously Amended) The method of claim 51, in which the microelectrode is planar or flexible.

56. (Previously Added) The method of claim 51, in which the microelectrode is a field effect transducer.

57. (Previously Amended) The method of claim 51, which further comprises an insulator layer surrounding the microelectrode selected from the group consisting of silicon, modified silicon dioxide, silicon nitride, silicon carbide, germanium, silica, gallium, arsenide, epoxy resin, polystyrene, polysulfone, alumina, silicone, fluoropolymer, polyester, acrylic copolymers, polylactate, or combinations thereof.

58. (Previously Added) The method of claim 51 in which said electrically active cell comprises a neuronal cell or a cardiac cell.

59. (Previously Added) The method of claim 58 in which the neuronal cell is a

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60. (Previously Added) The method of claim 51 in which the cell culture comprises a stem cell, a transformed stem cell, their respective progeny, or a combination thereof.

61. (Previously Amended) The method of claim 51 in which the stem cell is exposed to a differentiating factor.

62. (Currently Amended) The method of claim 51 in which ~~the surface-modifying agent~~ said intervening layer comprises a self-assembling monolayer or monolayers.

63. (Previously Added) The method of claim 62 in which the self-assembling monolayer comprises a silane, a thiol, isocyanide, polyelectrolyte or combinations thereof.

64. (Previously Added) The method of claim 51, wherein the intervening layer further comprises cell anchorage molecules selected from the group consisting of antibodies, antigens, receptor ligands, receptors, lectins, carbohydrates, enzymes, enzyme inhibitors, biotin, avidin, streptavidin, RGD-type peptides, integrins, cadherins, modified lipids, and combinations thereof.

65. (Previously Added) The method of claim 51, wherein the intervening layer further comprises a high viscosity mixture comprising alcohols, ethers, esters, ketones, amides, glycols, amino acids, saccharides, carboxymethylsaccharides, carboxyethylsaccharides, aminosaccharides, acylaminosaccharides, polymers thereof, or combinations thereof.

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66. (Previously Added) The method of claim 51 in which one or more cells are transfected with endogenous or exogenous nucleic acid.

67. (Currently Amended) The method of claim 66 in which the nucleic acid comprises a nucleotide sequence associated with known ~~or unknown~~ function.

68. (Previously Added) The method of claim 51, wherein the cell culture is coated with a polymer.

69. (Previously Added) The method of claim 68 in which the polymer comprises cellulose, methylcellulose, or dextran.

70. (Previously Amended) The method of claim 51, wherein a second layer is in contact with the electrically active cells and is attractive to cell adherence.

71. (Previously Added) The method of claim 51 in which the test substance comprises a toxin, a drug, a pathogen, a neurotransmitter, a nerve agent, or mixtures thereof.

72. (Previously Added) The method of claim 51 in which the deconvolution of cell membrane potential includes deconvoluting the cell action potential or its derivative.

73. (Cancelled) ~~The method of claim 72, in which deconvolution of the action potential or its derivatives provides information on pathways in the cell affected by the test substance.~~

74. (Currently Amended) The method of claim 51 ~~73~~, wherein ~~said~~ information on pathways in the cell ~~involves reference to~~ is derived using a data library of known compounds classified into one or more functional categories.

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75. (New) The method of claim 74, wherein said functional categories are phosphatidylinositol turn-over, calcium mobilization, phosphorylation of intracellular protein messengers, ion channel activators, ion channel blockers, transport proteins, binding proteins, cAMP formation, cell envelope and membrane function, cell regulatory functions, amino acid biosynthesis, fatty acid metabolism, phospholipid metabolism, steroid metabolism, glycolysis, cellular maintenance processes, gene expression, neurotransmission inhibitors, protein synthesis inhibitors, energy metabolism, transcription, translation, G-protein coupled receptor function, or receptor transduction.

76. (New) The method of claim 66 in which the nucleic acid comprises a nucleotide sequence associated with unknown function.